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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/554,704	08/15/2000	CATHARINA SVANBORG	032313-004	3220

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EXAMINER

ROBINSON, HOPE A

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 04/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/554,704	<b>Applicant(s)</b> SVANBORG ET AL.	
	<b>Examiner</b> Hope A. Robinson	<b>Art Unit</b> 1653	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 08 April 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-16 and 19-50 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1-16 and 19-50 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. The finality of the Office Action mailed January 8, 2004 is withdrawn in favor of the following Office Action.
2. Applicant's response to the Office Action mailed January 8, 2004 on April 8, 2004 is acknowledged.

### ***Claim Disposition***

3. Claim 50 has been added. Claims 17-18 were previously canceled. Claims 1-16 and 19-50 are pending and are under examination.
4. The following grounds of rejection are applicable:

### ***Claim Objections***

5. Claim 38 is objected to for the recitation of "Tris-HCl" instead of "TRIS (hydroxymethyl) aminomethane hydrochloride" to acknowledge and respect the trademark (see also claim 36 where TRIS is not capitalized).

### ***Specification***

6. The specification is objected to because of the following informalities:

The specification is objected to because on page 1 the priority information is missing.

The specification should be amended to recite:

This application is a 371 of PCT/IB98/01919 filed on November 23, 1998 and which claims priority to application numbers 9724725.8, filed on November 21, 1997 and 9812202.1, filed June 5, 1998. In addition, the specification is objected to because trademarks are disclosed and they are not capitalized. The use of the trademark such as TRIS®, has been noted in this application (see page 8, for example). It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks. It is suggested that the specification is amended to delete "Tris-HCl" and insert "TRIS (hydroxymethyl) aminomethane hydrochloride". The specification is also objected to for "ethylene diamine triacetic acid (EDTA)" instead of "ethylene diamine tetraacetic acid (EDTA)" see for example, pages 4-5. See also page 28, lines 4 and 11 where the word "cysteine" is misspelled as "cystein".

Correction is required.

### ***Claim Rejections - 35 U.S.C. § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

Art Unit: 1653

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 21-22, 37, 47 and 50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 21 is directed to a method wherein a cysteine residue of the alpha-lactalbumin is mutated to another amino acid and there is no indication in the claim as to which amino acid. Is it a D or L or Beta or Alpha or Gamma amino acid. The specification provides a brief discussion, which exemplifies the substitution of an alanine (see Example 11), however, the specification and claims do not describe all the other forms, which are encompassed in the broad claim language. The claims are also directed to "active component thereof" of a casein containing milk fraction" (see for example claim 22) and there is no indicia as to what active components are within the metes and bounds of the claims. The specification does not describe or exemplify said components.

Therefore a skilled artisan would have to engage in undue experimentation to determine what type of amino acid to substitute and once the mutant is constructed determine if the function is compromised or retained as the specification is missing adequate written description. Experimentation is necessary also to determine if the "component thereof" refers to a component of the casein, the milk or casein containing milk fraction, absent adequate guidance/direction. In addition, while it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited, as certain positions in the sequence are critical to the protein's structure/function relationship.

Thus, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 1-16 and 19-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite for the recitation of "said method results in the production of said biologically active oligomeric form" as the preamble of the claim is directed to "a method of producing a biologically active oligomeric form of alpha-lactalbumin", thus the claim lacks antecedent basis. It is suggested that the claim be amended to recite "said method results in the production of said biologically active oligomeric form of alpha-lactalbumin".

For clarity the phrases "a casein containing fraction obtainable from human milk" in claim 1; "a casein containing fraction derived from human milk" in claim 25 and "a casein containing milk fraction" in claims 37 and 43 should be amended to read "a milk fraction containing casein obtained from human milk". See also claim 22, which has similar language.

For clarity claim 2 should be amended to recite "contacted with the conversion reagent on an ion exchange column" instead of "contacted with the conversion reagent under conditions which allow ion exchange to take place" as it is unclear what ions or with what ions, to allow ion exchange. Note that this amendment will make claim 3 a substantial duplicate, therefore cancellation is suggested.

Claims 4 and 5 lack antecedent basis for the ion exchange column as claim two does not recite "an ion exchange column", nor claim 1, therefore, it is unclear when the conversion reagent in claim 5 is eluted.

Claim 7 is indefinite because the claim recites "a pretreatment step" and there is no indication of what is involved in the "pretreatment process". What is the alpha-lactalbumin subjected to in the pretreatment step?

Art Unit: 1653

For clarity claim 11 should be amended to delete the word "created" which means "shaped" regarding the pH. It is suggested that the claim be amended to recite "...wherein the pH of 2 is by addition of hydrochloric acid".

Claims 12 and 34 is indefinite because it is unclear as to how heating the alpha lactalbumin results in a temperature of from 25 degrees to 120 degrees as "25 degrees" is room temperature. It is suggested that the claims be amended to recite "...heating the alpha-lactalbumin from a temperature of 25 degrees to 120 degrees".

Claims 14 and 15 still lack antecedent basis as the claim recites "a molten globule inducing reagent" and the claims from which it depends recite "a conversion reagent", are these terms synonymous? In addition, the claims are indefinite for the recitation of "which will induce it", what is it? (See also claim 29). The dependent claim hereto is also included.

For clarity claim 15 should be amended to recite "...wherein the molten globule inducing reagent is a calcium chelating agent present in the elution buffer", deleting the phrase "which is", as this is not necessary in the claim.

Claim 16 is indefinite for the recitation of "ethylene diamine triacetic acid (EDTA) instead of "ethylene diamine tetraacetic acid (EDTA)" see for example claim 30.

Amended claim 20 is indefinite because the claim recites that the "calcium binding sites have been inactivated" and it is unclear how or with what the calcium binding sites are inactivated and there is no indication as to whether the inactivation is temporary or permanent. The dependent claims are also included.



Art Unit: 1653

Amended claim 21 is indefinite for the recitation of, "mutated to another amino acid" as there is no indication in the claim of which ones, for example, L amino acids, D amino acids, Beta, gamma or alpha.

Claim 22 is indefinite as to what the metes and bounds of the claim are with respect to the language "a casein containing fraction of milk or an active component thereof", is the active component thereof referring to the milk, the casein or the milk containing casein? It is suggested that applicant delete the phrase "active component thereof".

For clarity claim 24 should be amended to recite "in a purified form" in lieu of "in a pure form".

For clarity claim 26 should be amended to recite "...treated with a casein which has been previously frozen or obtained from frozen milk", deleting the phrase "containing milk fraction and is derived" as it is unclear if the milk was previously frozen or the casein and if so how derived?

Claim 31 has an improper sentence structure, the claim should be amended to recite "calcium chelating agent contacts the alpha-lactalbumin" instead of "calcium chelating agent is contacted with the alpha-lactalbumin".

For clarity claim 32 should recite "...wherein the calcium chelating agent contains an elution buffer and wherein said alpha-lactalbumin is contacted with said ion exchange medium", as the present claim wording does not achieve the effect of contact between the alpha-lactalbumin and the ion exchange medium.

Art Unit: 1653

Claim 37 is indefinite for the recitation of "...down the ion exchange column...".

Down in relation to a concentration affected by gravity or a concentration gradient?

What if the column is inverted?

Claim 39 lacks antecedent basis for "the salt", the claim should be amended to recite "said salt concentration gradient...".

Claim 45 lacks proper multiple dependent claim language, the claim should be amended to recite "according to any one of claims 43 or 44". Note however, that there is no antecedent basis for "ion exchange column", therefore, the claim should be amended to recite "ion exchange medium".

Claim 46 is indefinite as the claim recites "an oligomeric form of alpha-lactalbumin obtained by a method according to claim 1", an oligomeric form does not occur naturally, note that claim 1 recites a molten globule-like state.

Claim 47 is indefinite because the claim recites "the calcium binding site is destroyed" and it is unclear if the destruction is permanent.

Claim 50 is indefinite for the recitation of "mutated form of the native alpha-lactalbumin" because it is unclear what is the so-called "mutated form of the native". What is mutated? What is native? What is a mutated native? The claim is also indefinite for the recitation of "domains inactive" is the inactivity permanent or temporary and how does it become inactive? The claim is further indefinite for the recitation of "in a manner similar to oleic acid", what manner is similar to oleic acid?

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103 (a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103 (a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102 (f) or (g) prior art under 35 U.S.C. 103 (a).

Art Unit: 1653

10. Claims 46 and 48-49 are rejected under 35 U.S.C. 102(b) as been anticipated, or in the alternative, under 35 U.S.C. 103(a) as obvious over Jegouic et al. (Journal of Agricultural and Food Chemistry, vol. 45, no. 1, pages 19-22, January 1997).

Jegouic et al. teach baric oligomerization of alpha-lactalbumin that is treated with low-molecular weight reducing thiols (conversion reagents) see page 19, lines 1-5 of the introduction. This treatment partially unfolds the proteins and converts them into a molten globule-like state (reduction of the disulfide bonds, page 5 of the specification). The reference teaches that the contact between alpha-lactalbumin and the conversion agent (reducing thiols) is achieved under conditions, which would allow ion exchange to take place see pages 19-20 of the reference. This rejection has been made as a 102/103 rejection in view of the product-by-process format of the claims. The use of a 102/103 rejection for the rejection of a product-by-process claim has been approved by the courts. While the reference do not specifically disclose a fatty acid as a conversion agent as recited in the method of claim 1, the production of the oligomeric form of alpha lactalbumin (claims 46 and 48-49) by a particular process does not impart novelty or unobviousness to a protein when the same protein is taught by the prior art. This is particularly true when the properties of the protein are not changed by the process in an unexpected manner. See *In re Thrope*, 227 USPQ 964 (CAFC 1985); *In re Marosi*, 218 USPQ 289, 292-293 (CAFC 1983); *In re Brown*, 173 USPQ 685 (CCPA 1972).

Art Unit: 1653

11. Applicant's arguments filed on January 8, 2004 have been considered. Note that the rejections of record have been withdrawn and the above grounds of rejections have been instituted.

***Conclusion***

12. No claims are presently allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday from 9:00 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

  
CHRISTOPHER S. F. LOW  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600

Art Unit: 1653

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS 

Patent Examiner